phils to leukotriene B_4. Although much is still unknown regarding the role of the leukotrienes in inflammation, their potency and ubiquity make them strong candidates as inflammatory mediators or modulators in many disease processes involving recruitment of inflammatory cells. Present efforts are being directed toward the development of specific inhibitors of leukotriene formation. Such agents would be very useful for basic research on the interaction of arachidonic acid metabolites and of great therapeutic potential in the treatment of asthma, rheumatoid arthritis or other related conditions.

Elucidation of increasing numbers of surface receptors for diverse chemoattractants on neutrophils, together with the understanding that the various neutrophil functions are triggered by occupation of these receptors, provides basic information for a clearer understanding of neutrophil function in inflammatory conditions and will likely provide clinicians with more disease-specific and effective therapies in the near future.

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Clinical Significance of Helper/Suppressor T Cells

THE MORPHOLOGICAL determination (typing) of the percent and absolute number of circulating T-"helper" and -"suppressor" lymphocytes has gained widespread popularity with the development of monoclonal antibodies to detect antigens on the surface of different subpopulations of human lymphocytes. In this context, the terms T "helper" and "suppressor," which are functional terms, are gross oversimplifications. The helper T cells, as detected by the monoclonal antibodies in general use such as T4, contain not only helper cells for immunoglobulin synthesis but also inducer cells for many T-cell functions and even the precursors of some suppressor T cells. Thus, the T-helper/inducer population is really a mixture of related but distinct T cells. These distinctions based on function can be delineated immunologically by other monoclonal antibodies not in general use. Similarly, the suppressor T cells defined by monoclonal antibodies such as T8 comprise a variety of cell types involved in cytotoxicity and in inhibition of immune responses.

The measurement of helper and suppressor T-cell numbers, percents and ratios can be compared with the measurement of different types of leukocytes by differential cell count. Values may be abnormal in many cases but the clinical utility is limited to a very small number of disorders. Furthermore, while the test is very sensitive, it is also nonspecific, being altered in many infectious (especially viral), metabolic, neoplastic, rheumatologic and congenital and acquired immunologic disorders. Quantitation of helper/suppressor T cells may be clinically useful in certain suspected immunologic disorders. In infants, it can be used to distinguish between transient hypogammaglobulinemia (reduced helper T cells) and congenital agammaglobulinemia (normal helper/suppressor T cells and absent B cells). In adults, T-cell subsets are most often measured in the evaluation of persons suspected of having the acquired immune deficiency syndrome (AIDS). While a reduced number (and percent) of helper T cells with a normal or increased percent of suppressor cells is almost uniformly found in patients who have AIDS, these findings are very nonspecific and, in themselves, not diagnostic. Moreover, altered helper/suppressor T-cell ratios are found after a viral infection and in many sexually active homosexual men who do not have AIDS. Thus, while an abnormal helper/suppressor T-cell ratio is a characteristic immunologic finding useful in confirming the diagnosis of AIDS, it is by no means diagnostic of the disorder. In other adult immunodeficiencies, such as common variable immunodeficiency, T-cell subsets (by the generally used markers) are often abnormal but appear to have no relationship to the in vivo or in vitro functional defects observed.

Measurement of helper/suppressor T cells is not a screening test. In selected patients with possibly abnormal T-cell function, it should be used in conjunction with other tests of immune function such as a battery of delayed hypersensitivity skin tests. It is important to emphasize that patients should not be labelled as having an "immune disorder" or "dysfunction" solely on the basis of an in vitro morphologic determination of helper/suppressor T cells.

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Penicillin-Induced Anaphylaxis

OF AN ESTIMATED 400 to 800 anaphylactic deaths per year in the United States, as many as 75% have been ascribed to penicillin sensitivity. Anaphylaxis may occur in one to four instances per 10,000 patient treatment courses. The death rate is about 1 to 2 per 100,000 patients treated. The oral route appears to be the safest but reactions and even death have occurred from penicillin taken orally. Children are at lower risk than adults.

Penicillin is the only drug whose allergenic metabolites have been identified. The penicilloyl moiety, formed in largest quantity and thus called the major determinant, is responsible most often for accelerated urticarial reactions. A skin test reagent for detecting sensitivity to this determinant is available commercially as penicilloyl-poly-

lysine. Some ten other antigens comprise the minor determinants but test reagents for these are not available for routine use. IgE antibodies to penicilloate and other minor determinants are associated with anaphylactic sensitivity. Preformed conjugates and self-polymers that may be present in penicillin preparations are thought by some investigators to play a role in penicillin anaphylaxis.

The presence of penicillin-specific IgE is conveniently and rapidly shown by immediate wheal and erythema skin testing. Although sometimes a screening procedure, penicillin skin tests are usually done in patients who require penicillin for a serious infection and who have a history of penicillin allergy. Prick followed by intradermal tests is done with penicilloyl-polylysine, various concentrations of the aqueous fresh penicillin to be used and proper controls. Significant reactions to subsequently administered penicillin are unlikely in skin test-negative patients. Persons without a history of penicillin allergy have a 7% or less incidence of positive skin tests. Clinical histories suggestive of IgE-mediated reactions yield a 17% to 46% positive skin test rate, depending on the type of previous reaction and the time elapsed between the reaction and skin testing.

Past sensitivity wanes with time and future sensitization may occur anytime. Consequently, skin testing is relevant only to a current clinical situation. It is safe when properly done. In vitro testing for specific IgE to penicilloyl by radioallergosorbent test is promising because it would avoid the rare instance of reaction to skin testing, but it does not predict anaphylaxis.

In cases in which penicillin is still considered the drug of choice in the face of a positive skin test, desensitization may be done. Oral as well as parenteral methods have been proposed. Parenterally given desensitization is effective but cumbersome and can be associated with severe life-threatening reactions. Oral desensitization appears to be effective and relatively safe. It is usually accomplished with less severe reactions.

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Diseases of Cilia

THE SIGNIFICANCE of ciliated epithelium in both health and disease of the human respiratory tract has been increasingly appreciated. Mucociliary clearance, a process highly dependent on the coordinated metachronal movement of cilia, is an important mechanism for protecting the upper and lower airways. Both primary and secondary types of ciliary dysfunction have now been described.

A primary defect in the ultrastructure of cilia, normally represented as nine pairs of peripheral microtubules around two central ones, appears to be important in the pathogenesis of the immotile cilia syndrome, a hereditary disease clinically characterized by bronchiectasis, sinusitis and situs inversus in half the cases (termed Kartagener's syndrome when the latter is present). Cilia in this disorder have congenital abnormalities in the microtubular apparatus necessary for normal ciliary beating. The most common specific defect seen on electron microscopy is absence of the dynein arms—structures that facilitate intermicrotubular attachment and reattachment, resulting in bending of the cilium. Other ultrastructural variations include absence of the radial spokes and transposition of the microtubules. The diagnosis is usually made in adults with a history of chronic pulmonary or sinus disease (or both); some men present with infertility due to immotile sperm. Ultrastructural defects of cilia are also found in children who have not only the expected sinopulmonary problems, but also chronic otitis or a history of neonatal respiratory distress syndrome. One case of a different type of a primary ciliary abnormality, the isolated absence of nasal cilia, has been described. The affected boy had problems with persistent rhinitis and either chronic sinusitis or undeveloped sinuses.

Secondary or acquired disorders of cilia can occur due to various external influences inducing changes in ciliated respiratory epithelium. Ciliary dropout and damaged cilia along with decreased mucociliary clearance have been seen in patients who have allergic rhinitis after local nasal antigen challenge. Similarly, tracheal mucous transport rates, as measured by a technique using labelled Teflon particles, are diminished in patients with asthma, and antigen challenge causes further impairment. This dysfunction may be due to a ciliary inhibitory factor in sputum, possibly a leukotriene, though mucous changes are more likely to be the determining factor in asthma. Long-term cigarette smoking can lead to ciliary changes including swollen, compound cilia and even cilia with "9 plus 2" ultrastructural aberrations. Short-term cigarette smoke exposure can either diminish or enhance mucociliary clearance, the latter probably due to direct parasympathetic stimulation by nicotine. Chronic sulfur dioxide exposure, topical nasal decongestant use, aspirin administration and *Mycoplasma* infection have all been associated in humans or animals with either cilia detachment or decreased mucociliary activity, or both, thereby possibly compromising nasal and lung defense mechanisms.

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